Upon entry of the present Amendment, claims 17-25 will be pending in the instant Application.

THE REJECTIONS UNDER 35 U.S.C. §112, SECOND PARAGRAPH SHOULD BE WITHDRAWN

Claims 1-6 are rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention. In particular, the Examiner contends that the intended chimeric virus as claimed is not well defined. Further, the Examiner contends that for something to be chimeric it has to encompass distinct elements both of which have to be defined by their respective limitations.

In response, Applicants have canceled the claims and submit new claims in order to more distinctly point out the elements which constitute the chimeric virus of the claimed invention.

The Examiner further contends that the intended function of the chimeric virus is not present in the claim. First, Applicants respectfully point out that there is no legal requirement that the intended function or use[1] be recited in a claim. Further, Applicants respectfully point out that the present claims are composition claims and that any recitation of any intended function or use would not properly limit the claims. Thus, whether or not the claims recite any intended use or function should be without any consequence for the patentability of the claims of the present application.

The Examiner further contends that it is not clear what genes are being substituted, added, or deleted. Applicants respectfully point out that independent claim 17 recites heterologous sequences that are to be added or deleted to the backbone of the chimeric virus, and that dependent claims 18-21 further specify heterologous sequences that are to be added or substituted.

The Examiner further contends that it is not clear whether the claims are directed to a chimeric vector or a general parainfluenza expression vector. Applicants respectfully point out that the two alternatives put forward by the Examiner are not mutually

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[1] The Examiner writes in the Office Action that "...its intended function is not present." Based on the context, Applicants assume that the Examiner means that the claims do not recite the intended use of the chimeric virus.

exclusive. Rather, the claimed composition encompasses both, chimeric virus and expression vector. The chimeric virus is chimeric since it is composed of nucleotide sequences derived from a bovine parainfluenza virus type 3 genome and a heterologous sequence, *i.e.*, two distinct elements. Further, the chimeric virus can also be described as an expression vector since the heterologous sequence is to be expressed in a host cell.

The Examiner further contends that the position at which a heterologous sequence is to be inserted, is not specified in the claims. In response new claims 24 and 25 have been added to specify the nucleotide positions of Kansas-strain bovine parainfluenza virus type 3 at which the heterologous sequence is to be added.

The Examiner further contends that it is unclear what genes form the "backbone". Applicants respectfully point out that it is clear from the specification as originally filed that the backbone is formed by the nucleotide sequences of the genome of the Kansas-strain bovine parainfluenza virus type 3. For example, on page 30, lines 11-14, Applicants recite a backbone of "a ~14 kb DNA fragment encompassing all of the viral bPIV3 sequences except the F and HN genes".
Thus, the skilled artisan would understand that the "backbone" is formed by the nucleotide sequences of the genomes of Kansas-strain bovine parainfluenza virus type 3.

The Examiner further contends that the term "derived" renders the claims that recite it indefinite. In particular, the Examiner contends that " 'derived' is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of skill in the art would not be reasonably apprised of the scope of the invention." In response, without conceding the Examiner's contention, the term "derived" has been deleted from the claims. Thus the rejection should be mute with regard to the use of the term "derived".

The Examiner further contends that the intended heterologous sequences are not defined and that therefore the recitation of a heterologous sequence in a claim renders the claim indefinite. Applicants respectfully disagree and direct the Examiner's attention to the specification of the application as originally filed. On page 14, line 25 to page 18, line 11 of the application as originally filed, heterologous sequences for use with the invention are described.

The Examiner further contends that the intended "mutations or modifications" are not defined and that "enhanced antigenicity" and "modifications" are relative terms. Applicants respectfully disagree and point out that these terms are well-established in the art and would be clear to the skilled artisan. For example in the section entitled *Influenza* on page 95 of R. Spaete, 2001 (Recombinant Live Attenuated Viral Vaccines, In: New Vaccine Technology, Ronald W. Ellis (Editor), Eurekay.com, Austin, Texas; attached as Exhibit B; herein referred to as "Spaete, 2001"), the relevant state of the art for attenuated viruses at around the time of filing of the present application is described. It is well established in the art that certain mutations, see, *e.g.*, Spaete, 2001, cause an attenuated phenotype of the virus, thus giving rise to a virus that is more suitable for vaccine formulations. Further, in McCallus et al., 2001 (DNA Vaccines, In: New Vaccine Technology, Ronald W. Ellis (Editor), Eurekay.com, Austin, Texas; attached as Exhibit C; herein referred to as "McCallus et al., 2001"), the state of the art with respect to "enhanced antigenicity" is illustrated. In particular on page 254 of McCallus et al., 2001, examples of how antigens can be modified to achieve a heightened immune response are described.

THE REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH, SHOULD BE WITHDRAWN

Claims 1-6 are rejected under 35 U.S.C. §112, first paragraph, for alleged failure of the specification to provide enablement for the full scope of the claims. In particular, the Examiner contends that the "specification, while being enabling for bovine parainfluenza virus type 3 having its surface glycoproteins HN and F genes being substituted with HN and F glycoproteins of human parainfluenza virus type 3, forming a chimeric bPIV3/hPIV3 virus..., does not reasonably provide enablement for all types of chimeric viruses with bPIV3 'backbone' wherein all types of genes from all types of viruses would induce protective response (vaccine) or exhibit 'enhanced antigenicity' with any and all types of modifications."

Applicants respectfully assert that, for the reasons discussed below and according to the applicable case law, the instant specification does, indeed, fully enable one of skill in the art to make and use chimeric viruses corresponding to the scope of the presently pending claims.

THE LEGAL STANDARD

The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Telectronics Inc.*, 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988). In fact, well known subject matter is preferably omitted. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986) ("a patent need not teach, and preferably omits, what is well know in the art."). Further, one skilled in the art is presumed to use the information available to him in attempting to make or use the claimed invention. *See Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 941 (Fed. Cir. 1990) ("A decision on the issue of enablement requires determination of whether a person skilled in the pertinent art, using the knowledge available to such a person and the disclosure in the patent document, could make and use the invention without undue experimentation."). These enablement rules preclude the need for the patent applicant to "set forth every minute detail regarding the invention." *Phillips Petroleum Co. v. United States Steel Corp.*, 673 F. Supp. 1278, 1291 (D. Del. 1991); *see also DeGeorge v. Bernier*, 768 F.2d 1318, 1323 (Fed. Cir. 1985).

Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. *Fields v. Conover,* 170 USPQ 276, 279 (CCPA 1971). The factors that can be considered in determining whether an amount of experimentation is undue have been listed in *In re Wands,* 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Among these factors are: the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of pertinent literature and the level of skill in the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, so long as it is merely routine. *Id.*

Further, while the predictability of the art can be considered in determining whether an amount of experimentation is undue, mere unpredictability of the result of an experiment is not a consideration. Indeed, the Court of Custom and Patent Appeals has specifically cautioned that the unpredictability of the result of an experiment is not a basis to conclude that the amount of experimentation is undue in *In re Angstadt,* 190 USPQ 214 (CCPA 1976):

> [If to fulfill the requirements of 112, first paragraph, an applicant's] disclosure must provide guidance which will enable one skilled in the art to determine, with reasonable certainty before performing the reaction whether the claimed product will be obtained, . . . then all "experimentation" is "undue" since the term "experimentation" implies that the success of the particular activity is uncertain. Such a proposition is contrary to the basic policy of the Patent Act.

Id. at 219 (emphasis in the original).

THE INSTANT SPECIFICATION
PROVIDES AMPLE GUIDANCE TO THE SKILLED
ARTISAN FOR MAKING THE CLAIMED CHIMERIC VIRUSES

The instant specification, together with information which was readily available to the skilled artisan at the time the instant application was filed, provides a disclosure which fully enables the claimed invention.

Applicants respectfully point out that the specification as originally filed provides ample guidance for how to make the chimeric viruses. On page 18, line 13 to page 21, line 5 of the specification as originally filed, approaches for how to construct the chimeric viruses are described. Further Applicants respectfully point out that the skill in the field of Molecular Biology is very high. Thus the skilled artisan would have been able at the time of filing of the application to generate the claimed chimeric viruses. On page 22, line 16 to page 25, line 27, the specification discloses how to prepare the chimeric virus.

With regard to "how to use" the invention, the application as originally filed describes on page 21, line 28 to page 22, line 14 and from page 26, line 1 to page 30, line 2 how to use the chimeric viruses of the invention in a variety of different ways. In section 5.2 (page 21, line 28 to page 22, line 14), the specification describes how to use the chimeric viruses to express the gene products encoded by the heterologous sequences. On page 26, line 1 to page 30, line 2, the specification as originally filed describes how to use the chimeric viruses of the invention for vaccine formulations.

Further, Applicants respectfully point to the following passage of section 2164.01(c) of the MPEP:

> "[...] when a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a

> rejection for nonenablement based on how to use. If multiple uses for claimed compounds or compositions are disclosed in the application, then an enablement rejection must include an explanation, sufficiently supported by the evidence, why the specification fails to enable each disclosed use. In other words, if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention." (Emphasis added).

Applicants respectfully point out that the claimed invention relates to chimeric parainfluenza viruses which according to the specification as originally filed have many enabled utilities, including expression of heterologous sequences, in addition to use in vaccine formulations. Thus, Applicants have met the standard set forth in the aforementioned section of the MPEP by providing enablement for at least one utility. Even assuming *arguendo* that the vaccine formulations are not enabled for the entire genus, the Examiner fails to give any reason for lack of enablement for the use of the chimeric viruses to express the heterologous sequences. Thus, the Examiner has not met the requirement for showing a lack of enablement, and Applicants respectfully request that the rejection based on lack of enablement be withdrawn.

Further, the Examiner contends that "[t]he teaching of the specification is deficient in providing complete protection against any virus, there are no challenge study present that would show complete protection against any virus." In response, Applicants respectfully direct the Examiner's attention to another passage of section 2164.02 of the MPEP:

> "[...] if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate."

A vaccine gives rise to immunity to a particular pathogen in a subject. The generation of specific antibodies by the subject in response to administering the vaccine is one essential aspect of the immunity against the pathogen. Thus, it is an accepted view in the art that the generation of specific antibodies in response to administering a vaccine correlates with the generation of immunity against the pathogen. Accordingly in Example 9 of the specification as originally filed (page 32, line 28 to page 34, line 30), infection of hamsters with chimeric bPIV3/hPIV3 virus results in the production of antibodies specific to hPIV3 in those hamsters. That this is a well-established system in the art, and that the skilled artisan is

able to interpret the results of such an assay is exemplified in Crookshanks and Belshe, 1984 (J Med Virol, 13(3):243-249; attached as Exhibit D).

Further, Applicants respectfully point out that procedures for testing a vaccine are routine in the art, and that the skilled artisan would be able to determine without undue experimentation which of the chimeric viruses covered by the pending claims confer immunity to a subject when administered as a vaccine. In the context of this argument, the Applicants would like to direct the Examiner's attention to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing *In re Angstadt*, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)):

> " 'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.' "

Thus screening procedures to test chimeric viruses of the invention for their potential to serve as vaccines and to confer immunity to a particular pathogen to a subject should not be considered undue experimentation since such procedures are well-known to the skilled artisan.

Applicants respectfully request that the rejections under 35 U.S.C. § 112, first and second paragraphs, of claims 1-6 be withdrawn.

THE REJECTIONS UNDER 35 U.S.C. § 102 SHOULD BE WITHDRAWN

The Examiner has rejected claims 1-6, which are drawn to chimeric parainfluenza viruses as anticipated by Murphy et al (WO 98/53078; "Murphy"). In particular, the Examiner points out that Murphy teaches "[...] that a bovine parainfluenza virus may be modified to comprise heterologous genes including glycoproteins that can be substituted from human PIVs that would induce an immunogenic response."

Applicants respectfully point out that the claims as currently pending are directed to chimeric viruses comprising sequences encoding a Kansas-strain bovine parainfluenza virus type 3 in addition to heterologous sequences. Murphy describes modifications to the genome of a bovine parainfluenza virus but does not specifically describe such modifications of the Kansas-strain of bovine parainfluenza virus type 3.

Applicants direct the Examiner's attention to the following passage of section 2132.02 of the MPEP:

> "A genus does not always anticipate a claim to a species within the genus. However, when the species is clearly named, the species claim is anticipated no matter how many other species are additionally named."

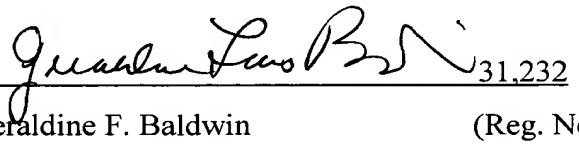
As Murphy does not describe the Kansas-strain, which is a species of the genus of bovine parainfluenza virus, Murphy cannot anticipate the instant claims. Thus, Applicants respectfully request that the rejection under 35 U.S.C. § 102 be withdrawn.

CONCLUSION

Applicants respectfully request that the amendments and remarks of the present response be entered and made of record in the instant application. Withdrawal of the Examiner's rejections and an allowance of the application are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

Date: May 7, 2002



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Enclosures

EXHIBIT A
PENDING CLAIMS AFTER ENTRY OF THE AMENDMENT FILED ON MAY XX, 2002
U.S. PATENT APPLICATION SERIAL NO. 09/531,375

17. (new) A chimeric parainfluenza virus comprising:

(i) nucleotide sequences of a Kansas-strain bovine parainfluenza virus type 3 genome; and

(ii) one or more heterologous sequences, wherein said one or more heterologous sequences have been added to said virus genome or have been substituted for nucleotide sequences of said virus genome.

18. (new) The chimeric parainfluenza virus of claim 17, wherein the heterologous sequences are that of a human parainfluenza virus.

19. (new) The chimeric parainfluenza virus of claim 18, wherein the heterologous sequences encode the F and HN glycoproteins of a human parainfluenza virus.

20. (new) The chimeric parainfluenza virus of claim 19, wherein the F and HN glycoproteins of an hPIV are that of a human parainfluenza virus type 3.

21. (new) The chimeric parainfluenza virus of claim 17, wherein the heterologous sequences are that of an influenza virus or of a respiratory syncytial virus.

22. (new) The chimeric parainfluenza virus of claim 17, wherein the Kansas-strain bPIV3 backbone contains mutations or modifications, in addition to heterologous sequences, which result in a chimeric virus having a phenotype more suitable for use in vaccine formulations such as an attenuated phenotype or a phenotype with enhanced antigenicity.

23. (new) A chimeric parainfluenza virus comprising:

(i) the genome of Kansas-strain bovine parainfluenza virus type 3; and

(ii) one or more heterologous sequences, wherein said one or more heterologous sequences have been added to said backbone.

24. (new) The chimeric parainfluenza virus of any one of claims 17-23, wherein said heterologous sequence substitutes both the F and the HN gene of Kansas-strain bovine parainfluenza virus type 3.

25. (new) The chimeric parainfluenza virus of any one of claims 17-23, wherein said heterologous sequence is added at a nucleotide position of Kansas-strain bovine parainfluenza virus type 3 selected from the group consisting of nucleotide position 5041, the HN gene, and nucleotide position 8529.